

Keith Phillips^a
David A. Howard^a
Mark C. Bentley^a
Gunnar Alván^b

^a Department of Air Quality Monitoring,
Covance Laboratories Ltd., Harrogate, UK;
^b Karolinska Institute, Department of
Medical Laboratory Sciences and
Technology, Division of Clinical
Pharmacology, Huddinge University
Hospital, Huddinge, Sweden

Environmental Tobacco Smoke and Respirable Suspended Particle Exposures for Non-Smokers in Beijing

Key Words

Air quality
Nicotine
Solanesol
Cotinine
Cigarette equivalents
Personal monitoring

Abstract

The study was centred in Beijing, People's Republic of China, and comprised housewives in one group, primarily for assessing exposures in the home, and office workers in a second group to assess the contribution of the workplace to overall exposure. Two hundred and fifty-three randomly selected non-smoking subjects collected air samples near to their breathing zone by wearing personal monitors for 24 h. Samples collected were analysed for respirable suspended particles (RSP), nicotine, 3-ethenylpyridine and environmental tobacco smoke (ETS) particles using ultraviolet absorbing particulate matter (UVPM), fluorescing particulate matter (FPM) and solanesol-related particulate matter (SolPM) measurements. Saliva cotinine analyses were also undertaken to confirm the non-smoking status of the subjects, and a misclassification rate of between 3.4 and 3.8% was estimated. RSP levels were the highest reported to date by these authors, with median 24-hour time-weighted average concentrations varying between $70 \mu\text{g}\cdot\text{m}^{-3}$ for housewives living in non-smoking households and $114 \mu\text{g}\cdot\text{m}^{-3}$ for office workers both living and working in smoking environments. High background levels of unidentified airborne fluorescing compounds in Beijing resulted in abnormally high FPM estimates and precluded the use of this marker in the assessment of ETS exposure. The highest exposures to ETS particles (SolPM) and nicotine were estimated for office workers living and working in smoking environments. These subjects would potentially inhale between 5 and 11 cigarette equivalents per year (CEs/y), based upon median exposures, with the workplace contributing approximately 40% of this exposure. The most highly exposed subjects in this study, based upon 90th percentile exposures, would potentially inhale between 32 and 46 CEs/y.

RWLP0188

KARGER

Fax +41 61 306 12 34
E-Mail karger@karger.ch
www.karger.com

© 1999 S. Karger AG, Basel
1420-325X/98/0076-0254\$17.50/0

Accessible online at:
<http://BioMedNet.com/karger>

Mr. K. Phillips
Head of Air Quality Monitoring, Covance Laboratories Ltd., Otley Road
Harrogate, North Yorkshire HG3 1PY (UK)
Tel. +44 1423 500011, Fax +44 1423 508745
E-Mail keith.phillips@covance.com

PM3006485041

Introduction

Beijing, the capital city of China, is situated in the North East of the country and is a political, economic, cultural and transportation centre with an urban population of nearly 7 million. Over the past 2 decades, economic growth in China has outstripped the rest of the world, rapid industrial expansion being achieved with consequential detrimental effects upon the environment. A large amount of the country's air pollution results from the burning of coal, which is used to generate approximately 80% of the nation's electricity. Coal is also widely available to the general population and is the only source of heating and cooking in many households. Air pollution in Beijing is exacerbated by industrial pollution from the suburbs, wind-blown sand from nearby arid regions, large-scale rebuilding works throughout the city and a vehicle population of approximately 1 1/4 million, increasing by 15% per annum. The China Daily newspaper reported on 15th November 1997 that 89% of inhabitants were dissatisfied or very dissatisfied with Beijing's environmental quality, with air pollution listed as the top problem. In the last few years, the Chinese authorities have been attempting to address environmental issues with a wide range of schemes and have set ambitious targets for sustainable development by early next century. During 1997, measures were implemented within the city of Beijing in an attempt to improve air quality, these included bans on the sale of leaded petrol, the use of coal-fired cooking stoves in the streets and smoking in public places.

Beijing was the fourth Asian Pacific city investigated by the authors, following on from Hong Kong, Kuala Lumpur and Sydney [1-3]. Air quality investigations have already been reported for the European cities Stockholm, Barcelona, Turin, Paris, Bremen, Lisbon, Basel and Prague [4-11].

This study set out to assess the exposure of non-smokers in Beijing to respirable suspended particles (RSP) and environmental tobacco smoke (ETS) over 24-hour periods during October and November 1996. Personal monitoring was chosen in preference to static or ambient measurements in order to represent more accurately personal exposures to selected pollutants. The main objective of this study was to determine accurately exposures to RSP and ETS for housewives and office workers in Beijing, to be achieved by: (1) recruiting subjects into six separate groups (Cells), by random selection from a database representative of the population of Beijing; (2) determining the range and degree of personal exposure of these Cells of

selected subjects to RSP and ETS constituents; (3) assessing the overall contribution of the workplace to ETS and RSP exposure.

ETS particles were estimated using ultraviolet-absorbing particulate matter (UVM), fluorescing particulate matter (FPM) and solanesol-related particulate matter (SolPM). Vapour-phase ETS exposures were also assessed by simultaneous measurement of nicotine and 3-ethenylpyridine (3-EP) concentrations. Subjects were assigned into Cells based upon the smoking status of their households and workplaces. Households were classified as 'smoking' if a smoker of cigarettes, pipes or cigars was resident and also normally smoked within communal areas of the household. The smoking status of a workplace was defined by the absence/presence of smoking co-workers within 30 m of the subject's workstation. These definitions were chosen to represent best 'real-world' situations and to give consistency across the studies of the other cities, since the attitudes of the residents vary considerably from country to country. Subjects provided saliva samples for cotinine analysis and also self-reported activities using diaries and questionnaires. Similar methodologies have been used in a number of other recent studies [12-15].

Methods

Recruitment of Subjects

Recruitment was performed by Survey Research Group China, a leading Asian marketing company, which possesses one of the most complete personal databases in the region. A random sample population was selected from the database to comply with the following criteria: (1) all subjects to be non-smokers living within 15 km of Beijing city centre; (2) equal numbers in three age groups: 20-34, 35-49 and 50-64; (3) subjects' lifestyles to be representative of the population within 15 km of the city centre; (4) subjects to be distributed between six 'Cells' as indicated in table 1, with office workers targeted for Cells 3-6.

Subjects were recruited from randomly selected addresses and were screened by telephone to confirm eligibility for participation in the study. Suitable volunteers were given an appointment to attend an information/training session organised at the Holiday Inn Crowne Plaza, a centrally located hotel in Beijing.

The Monitoring Session

Subjects were required to wear a personal monitor, designed to collect particulate and vapour-phase components present in the air close to their breathing zone [16]. RSP and ETS particles were collected onto a Fluoropore membrane filter, nicotine and 3-EP were adsorbed onto XAD-4 resin beads. The personal monitoring methodology has been described in detail elsewhere [4] and was briefly as follows.

Initial Visit to the Study Centre. On arrival, subjects were shown an instructional video, dubbed into Mandarin, which explained the

Table 1. Cell categorisation by home and workplace status

Cell	Study type	Smoking status		Target
		household	workplace	
1	single monitor	smoking	—	55
2	single monitor	non-smoking	—	40
3	dual monitor	smoking	smoking	45
4	dual monitor	smoking	non-smoking	30
5	dual monitor	non-smoking	smoking	40
6	dual monitor	non-smoking	non-smoking	30

Table 2. LOQ for the analytical methods

Measurement	Analytical LOQ	LOQ expressed as air concentration according to sampling time, $\mu\text{g} \cdot \text{m}^{-3}$ ^a			Proportion of data below the LOQ, %
		24 h	15.9 h ^b	7.8 h ^c	
RSP	45.2 $\mu\text{g}/\text{filter}$	18.2	27.5	55.9	9
UVPM	1.23 $\mu\text{g}/\text{filter}$	0.50	0.75	1.5	1
FPM	0.29 $\mu\text{g}/\text{filter}$	0.12	0.18	0.36	0
SolPM	0.65 $\mu\text{g}/\text{filter}$	0.26	0.39	0.80	26
Nicotine	0.1 $\mu\text{g}/\text{tube}$	0.09	0.13	0.27	14
3-EP	0.1 $\mu\text{g}/\text{tube}$	0.09	0.13	0.27	37
Saliva cotinine	1.0 $\text{ng} \cdot \text{ml}^{-1}$	—	—	—	53

^a A flow rate of $1.72 \text{ l} \cdot \text{min}^{-1}$ through the Fluoropore filter was assumed in the LOQ calculation for RSP, UVPM, FPM and SolPM. The LOQ calculation for nicotine and 3-EP assumed a flow rate of $0.8 \text{ litres} \cdot \text{min}^{-1}$ through the XAD-4 tube.

^b Mean time spent outside the workplace for working subjects in Beijing.

^c Mean time spent at work for working subjects in Beijing.

objectives of the air quality survey. They were also given further instructions by locally recruited interpreters regarding use of the equipment and how to complete the documentation. Subjects were issued with Mandarin language questionnaires and diaries for recording air quality observations over the 24-hour collection period and were supervised during completion of the 'first-visit' questionnaire. In order to avoid misinterpretation and possible errors in translation, all questionnaires and diaries were designed for either numeric or tick-box answers. Non-working subjects recruited for participation in Cells 1 and 2 were provided with a single personal monitor for use over the collection period (single-monitor study). Working subjects recruited for participation in Cells 3–6 were provided with two personal monitors for use over the same period (dual-monitor study). All subjects were required to provide a saliva sample prior to the monitoring period (pre-sample).

Final Visit to the Study Centre. Following completion of the 24-hour monitoring period, subjects returned their personal monitors and associated documentation to the study centre. Subjects also provided a second saliva sample (post-sample), completed a 'last-visit' questionnaire and received a gratuity as compensation for their inconvenience.

Analytical Procedures

All analytical procedures were validated and have been fully described previously by the authors [4]. In this study, the following analytes were determined: (1) RSP – using a gravimetric procedure [17]; (2) saliva cotinine – using a radioimmunoassay procedure [18]; (3) nicotine and 3-EP – using a capillary gas chromatography procedure with nitrogen-specific detection [19]; (4) estimation of ETS particles (3 procedures) – using high-performance liquid chromatography procedures to determine UVPM, FPM or SolPM of methanolic filter extracts [4, 17]. The factors used in this study to convert instrument responses into an equivalent concentration of ETS particles were 43 (SolPM), 45 (FPM) and 8.2 (UVPM), as determined by Nelson et al. [20].

The analytical limits of quantification (LOQ) for these analyses are presented in table 2, together with the proportion of data below the LOQ. The analytical LOQ for RSP (45.2 μg) was calculated from the weights of blank samples [4] and was somewhat higher than those found in other cities in this series of studies (mean 23.6 μg). The reasons for the high LOQ were not fully investigated as the proportion of data below the LOQ (8.9%) was lower than that found in the majority of other cities studied (mean 17.2%). It was therefore believed that

Table 3. Age and sex distribution for study subjects

Cell	Sex		Age range			Overall total
	males	females	20-34	35-49	50-64	
1 (SH)	-	56	16	20	20	56
2 (NSH)	-	46	8	9	29	46
3 (SH, SW)	21	25	18	18	10	46
4 (SH, NSW)	10	21	13	14	4	31
5 (NSH, SW)	30	17	19	19	9	47
6 (NSH, NSW)	13	14	10	9	8	37
Single-monitor total		102	24	29	49	102
Dual-monitor total	74	77	60	60	31	151
Overall total	74	179	84	89	80	253

SH = Smoking household; NSH = non-smoking household; SW = smoking workplace; NSW = non-smoking workplace.

the higher LOQ for RSP in Beijing would have no significant effect upon the reported results. In order to calculate summary statistics for all analytes, any data below the analytical LOQ were assigned a value of $\frac{1}{2}$ LOQ prior to the calculation of air concentrations using the appropriate air sampling volume. The LOQ expressed as air concentrations in table 2 are therefore only an approximation as they varied for each sample depending upon the sampling pump flow rate and monitoring time. It should be recognised that the application of $\frac{1}{2}$ LOQ values precludes the assignment of a 'zero' air concentration, thus causing an apparent exposure concentration of all analytes in all locations. In the Cells where the majority of data were below the LOQ, median reported values could either underestimate (where data were close to the LOQ), or overestimate (where data were close to zero) the 'true' concentrations.

Results and Discussion

Subject Recruitment

Of the 265 subjects that were initially recruited for the study, 1 was excluded after admitting to smoking during the sampling period. A further 2 subjects were excluded as they had operated the monitoring equipment incorrectly during the sampling period and 9 subjects were excluded because their saliva cotinine levels were above the selected threshold ($25 \text{ ng} \cdot \text{ml}^{-1}$) for non-smokers.

The age and sex distributions of the remaining 253 subjects who successfully completed the study are presented in table 3. The sex distribution was very close to the planned 50% per sex for office workers in the dual-monitor study (49% male, 51% female). The age distribution for office workers showed some variation from the planned 33% for each age group, with 79% of the recruits falling into the two youngest (20-34 and 35-49 years) age

Table 4. Occupations of recruited working subjects

Occupation	Responses
Administrative/secretarial	48
Building/construction	3
Education	5
Engineering	9
Government agency (civil service)	23
Legal/financial (e.g. solicitor, banker)	17
Hotel/restaurant/leisure industry	4
Medical (e.g. doctor, nurse)	4
Wholesale/retail (e.g. shop assistant)	6
Science/computing	15
Supply industry	2
Transportation/haulage	0
Other	12
Total	148

groups. This trend was reversed for housewives in the single-monitor study, where 76% of the recruits were aged between 35 and 64 years. The dual-monitor study participants were also questioned about their occupation on the 'first-visit' questionnaire. Subjects were restricted to a choice of 13 options from which to select and provide their answers as summarised in table 4.

Verification of Non-Smoking Status

Saliva cotinine levels were determined in order to verify that recruited subjects had correctly reported themselves as non-smokers. In this study, $25 \text{ ng} \cdot \text{ml}^{-1}$ (maxi-

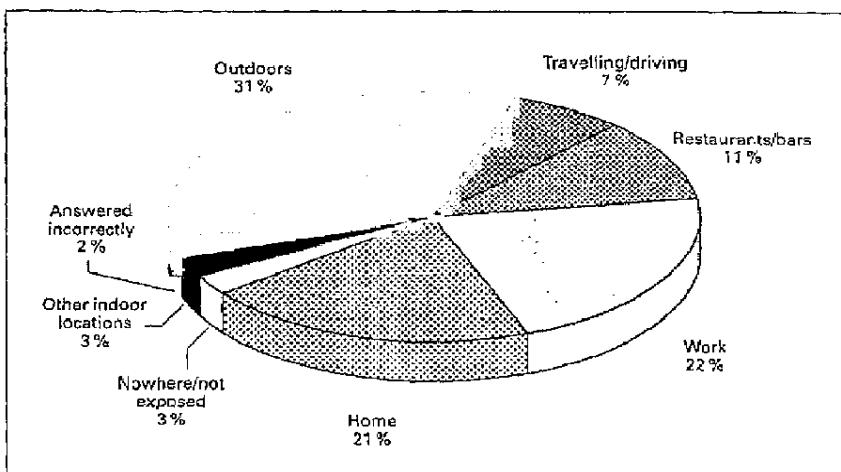


Fig. 1. Subjective responses to question: 'In which environment do you think that you are exposed to the *most* tobacco smoke in the air?'.

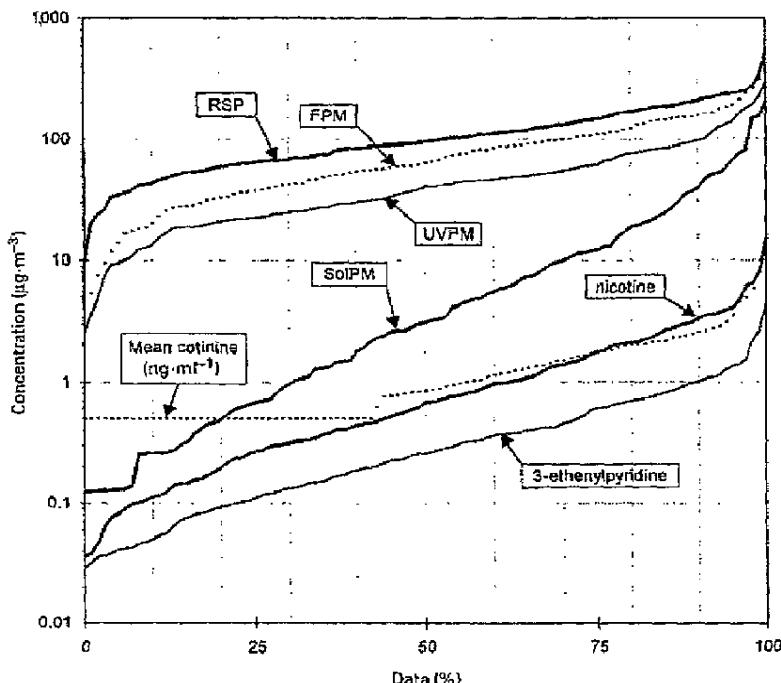


Fig. 2. Cumulative frequency distributions of all environmental tobacco smoke 'marker' concentrations.

imum of pre- and post-levels) was chosen as a suitable cut-off level to differentiate between smokers and non-smokers, a level used and described previously in a British study [21]. Using this threshold, 9 subjects with a concentration of cotinine between 25.5 and 121 $\text{ng} \cdot \text{ml}^{-1}$ (median 53 $\text{ng} \cdot \text{ml}^{-1}$) were assumed to be smokers and were ex-

cluded from the study. A further subject was excluded after admitting to smoking during the sampling phase of the study.

Previously, we have discussed some of the various criteria used to assess the rate at which recruited subjects misreport their smoking status [6]. Depending upon the

Table 5. Correlation coefficients for ETS 'markers' using only data greater than the LOQ

'Y' data	vs.	'X' data	Data pairs	R ²	Gradient	Intercept
FPM		UVPM	391	0.745	1.16	20.8
SolPM		UVPM	294	0.703	0.65	-20.8
SolPM		FPM	294	0.350	0.35	-13.0
3-EP		nicotine	241	0.742	0.18	0.34
FPM		nicotine	330	0.086	5.85	79.4
SolPM		nicotine	276	0.480	10.3	0.43
UVPM		nicotine	329	0.227	7.15	45.6
SolPM		3-EP	222	0.516	40.7	-6.85
FPM		3-EP	241	0.143	34.2	69.8
Post-cotinine		SolPM ^a	83	0.136	0.020	1.90
Post-cotinine		FPM ^a	115	0.024	0.004	1.94
Post-cotinine		nicotine ^a	97	0.368	0.44	1.34
Post-cotinine		3-EP ^a	74	0.415	1.64	1.08

^a TWA concentrations used for working subjects (Cells 3-6) having results from both the 'workplace' and 'outside of the workplace' monitors greater than the LOQ.

criteria used, the rate at which subjects misclassified their smoking status in this study ranged between 3.4% (9 from 262) and 3.8% (10 from 263).

Subjective Comparisons of ETS Exposure

As part of the 'last-visit' survey, the participants were asked a number of subjective questions regarding their exposure to ETS, both in general and during the 24-hour monitoring period. The environments assessed by subjects as being the single location where they were most exposed to ETS are depicted in figure 1. This shows that the largest percentage of recruited subjects believed that they were most exposed whilst outdoors. The same observation was apparent in the other Asian cities studied by us, but was somewhat different to the findings for the European cities, where outdoor locations were not perceived as a major source of ETS. The perception of outdoors being the major source of ETS exposure is likely to be a reflection of the generally poor air quality in Beijing. The indoor location generally perceived to contribute most to ETS exposure was the workplace, closely followed by the home. In all other cities studied by the authors, restaurant or bar areas were considered to be the places with highest indoor ETS exposures. Bars and restaurants are less common in Beijing, which may explain why subjects in this study perceived low ETS exposure in these locations.

Comparison of 'Markers' for Estimating ETS Concentrations

Cumulative frequency distributions for all analytes measured in this study are presented in figure 2 and show an overall trend of RSP > FPM > UVPM > SolPM for the particulate matter determinations. This trend differs from the expected trend of RSP > UVPM > FPM > SolPM [17], suggesting the presence of higher levels of fluorescing compounds in the particulate phase than have been observed previously by the authors.

The correlation and best-fit line coefficients between various analytes, after removal of data pairs where either analyte was below the LOQ, are listed in table 5. In contrast to previous studies, only a moderate correlation ($R^2 = 0.75$) was found between UVPM and FPM estimates. Additionally, SolPM was better correlated with UVPM ($R^2 = 0.70$) than with FPM ($R^2 = 0.35$). In previous cities studied by the authors, median FPM levels for the various Cells have been an average of 3.6 times higher than corresponding SolPM levels. In this study, the ratio of median FPM/SolPM was at an average of 41 for the six Cells investigated. These calculations indicate the presence of high levels of non-tobacco-related fluorescing compounds in the air in Beijing during the study. No attempt was made to identify the fluorescing compounds or to determine their origin, but likely sources are the high domestic and commercial use of coal, together with general industrial pollution.

Post-cotinine concentrations were poorly correlated with particulate-phase ETS measurements and only

Table 6. Twenty-four-hour TWA particle concentrations for all subjects

Analyte, µg·m ⁻³	Cell	Subjects	10th percentile	90th percentile	Arithmetic mean	Geometric mean	Median
RSP	1 (SH)	56	38	221	123	100	102
	2 (NSH)	45	26	161	84	69	70
	3 (SH, SW)	43	57	241	134	117	114
	4 (SH, NSW)	28	48	198	111	99	93
	5 (NSH, SW)	45	57	188	113	101	100
	6 (NSH, NSW)	25	44	226	119	92	95
SolPM	1 (SH)	56	0.28	67	22	5.1	8.3
	2 (NSH)	45	0.13	2.9	3.4	0.58	0.55
	3 (SH, SW)	44	2.2	70	29	11	12
	4 (SH, NSW)	28	0.68	24	10	4.2	3.3
	5 (NSH, SW)	46	0.54	38	12	4.6	4.9
	6 (NSH, NSW)	26	0.26	5.3	2.7	0.91	0.80
FPM	1 (SH)	56	19	164	99	65	60
	2 (NSH)	45	12	120	64	47	60
	3 (SH, SW)	44	30	216	100	76	75
	4 (SH, NSW)	27	20	147	79	65	74
	5 (NSH, SW)	46	29	140	79	64	72
	6 (NSH, NSW)	26	22	115	74	57	69
UVPM	1 (SH)	56	12	130	59	42	44
	2 (NSH)	45	9.4	59	32	25	26
	3 (SH, SW)	44	22	177	73	53	49
	4 (SH, NSW)	28	20	98	51	42	44
	5 (NSH, SW)	46	19	84	50	39	42
	6 (NSH, NSW)	26	11	74	37	29	31

TWA concentrations, determined for each subject from measured levels both inside and outside the workplace, were used to calculate the above statistical parameters for Cells 3–6.

SH = Smoking household; NSH = non-smoking household; SW = smoking workplace; NSW = non-smoking workplace.

slightly better with the vapour-phase markers, nicotine and 3-EP. These poor correlations may be due to the large proportion of the results close to the LOQ, where acceptable assay reliability is at a minimum. It was observed that both cotinine and SolPM correlated slightly better with 3-EP than with nicotine, possibly highlighting the suitability of 3-EP [22] as an ETS marker. Considerable benefits may be gained by the development of robust analytical methods, with considerably improved sensitivity, for both cotinine and 3-EP; currently many determinations for these analytes are close to or below the LOQ.

Concentrations of ETS Constituents to Which Beijing Subjects Were Exposed

In this paper, median values have been used for reporting RSP and ETS marker concentrations, since the data

generated were highly skewed. Additionally, arithmetic and geometric means have been quoted together with 10th and 90th percentile values for each data set. ETS particle exposures, corresponding cigarette equivalent (CE) calculations and comparisons between subject groups and Cells have been based solely upon SolPM determinations. Previously, these authors have suggested that SolPM values may underestimate ETS particle concentrations at low levels [6] and have also published data based upon FPM values for comparison. The requirement for careful data review and the use of multiple 'markers' in ETS exposure studies are highlighted by the fact that median FPM levels recorded in Beijing were higher than those recorded in any comparable study to date. For this study, it was considered inappropriate to calculate ETS particle exposures from FPM measurements due to the high level

Table 7. Cotinine and 24-hour TWA nicotine and 3-EP concentrations for all subjects

Analyte	Cell	Subjects	10th percentile	90th percentile	Arithmetic mean	Geometric mean	Median
Nicotine µg·m ⁻³	1 (SH)	54	0.19	3.6	1.7	0.92	1.3
	2 (NSH)	44	0.05	0.72	0.38	0.18	0.15
	3 (SH, SW)	42	0.58	4.6	2.5	1.8	1.8
	4 (SH, NSW)	25	0.26	2.4	1.2	0.80	0.91
	5 (NSH, SW)	45	0.33	2.8	1.3	0.82	0.77
	6 (NSH, NSW)	26	0.10	0.83	0.34	0.25	0.25
3-EP µg·m ⁻³	1 (SH)	54	0.06	1.00	0.53	0.32	0.38
	2 (NSH)	44	0.04	0.24	0.13	0.08	0.06
	3 (SH, SW)	42	0.25	1.3	0.82	0.59	0.53
	4 (SH, NSW)	25	0.11	0.80	0.41	0.30	0.32
	5 (NSH, SW)	45	0.14	0.91	0.44	0.31	0.28
	6 (NSH, NSW)	26	0.08	0.59	0.21	0.15	0.11
Cotinine ^a ng·mL ⁻¹	1 (SH)	56	0.50	2.5	1.4	1.1	1.0
	2 (NSH)	46	0.50	1.3	0.7	0.62	0.50
	3 (SH, SW)	45	0.50	4.1	2.2	1.6	1.9
	4 (SH, NSW)	31	0.50	2.5	1.4	1.0	0.93
	5 (NSH, SW)	46	0.50	2.3	1.2	0.94	0.81
	6 (NSH, NSW)	27	0.50	2.1	1.5	0.84	0.50

TWA concentrations, determined for each subject from measured levels both inside and outside the workplace, were used to calculate the above statistical parameters for Cells 3-6.

SH = Smoking household; NSH = non-smoking household; SW = smoking workplace; NSW = non-smoking workplace.

^a Values calculated from the average of pre- and post-monitoring saliva cotinine concentrations.

of 'interference' from other sources. A future approach for monitoring ETS exposure may be to identify additional tobacco-specific particulate-phase compounds, and to develop more sensitive and specific analytical methodologies than those currently available for solanesol.

Particulate- and vapour-phase components measured for housewives were compared, by Cell, with calculated time-weighted average (TWA) concentrations for individual workers. These calculations were based on measured concentrations and the operational time over which the monitors were used inside and outside the workplace. These data are summarised in tables 6 and 7, with corresponding cumulative frequency distributions for SolPM and nicotine shown in figures 3 and 4. A generalised overview of these data suggests that levels for all analytes were highest in the group with two known ETS exposure sources (Cell 3). Conversely, the levels of all analytes, with the exception of FPM, were lowest in the groups with no known ETS exposure (Cells 2 and 6). It can also be seen that the ratios of median concentrations for Cell 3 versus

either Cells 2 or 6 were in the order SolPM > nicotine > 3-EP > cotinine > UVPM > RSP > FPM. This may be taken to be the order of specificity of the various analytes to ETS in Beijing.

As the data were not normally distributed, the significance of any concentration differences between Cells was examined using the non-parametric Wilcoxon rank sum test. Prior to the application of this test, Kruskal-Wallis non-parametric analysis of variance (ANOVA) was applied to the data in order to ensure that there was an overall difference between the Cells. For FPM, the overall Kruskal-Wallis analysis proved non-significant ($p > 0.05$) and the Wilcoxon rank sum test was not performed as there would have been the possibility of false positives. The lack of any statistical difference in FPM concentrations between the six Cells indicates the presence of high background concentrations which masked any effects related to the presence or absence of tobacco smoke. This observation further highlights the unsuitability of FPM as an ETS marker in this study and may also indicate the

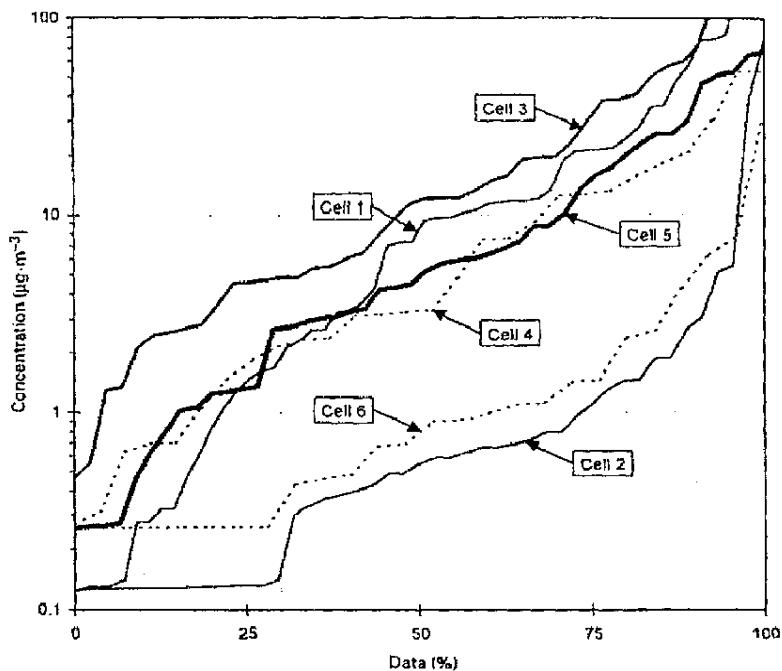


Fig. 3. Cumulative frequency distributions of ETS particle (SolPM) concentrations. Cell 1 = smoking home; Cell 2 = non-smoking home; Cell 3 = smoking home/smoking workplace; Cell 4 = smoking home/non-smoking workplace; Cell 5 = non-smoking home/smoking workplace; Cell 6 = non-smoking home/non-smoking workplace.

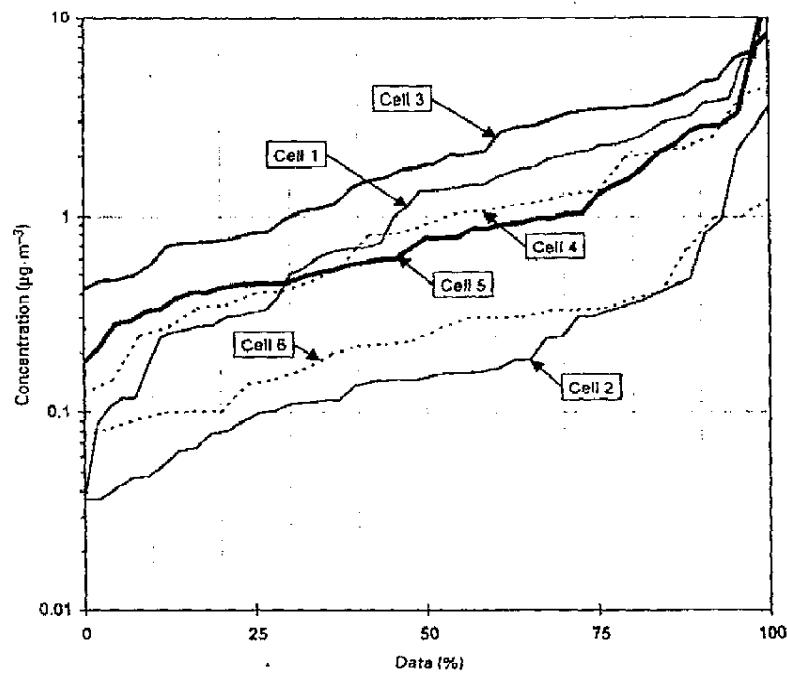


Fig. 4. Cumulative frequency distributions of nicotine concentrations. Cell 1 = smoking home; Cell 2 = non-smoking home; Cell 3 = smoking home/smoking workplace; Cell 4 = smoking home/non-smoking workplace; Cell 5 = non-smoking home/smoking workplace; Cell 6 = non-smoking home/non-smoking workplace.

Table 8. Significance of differences in ETS marker concentrations between Cells based upon Kruskal-Wallis ANOVA and subsequent Wilcoxon rank sum test

		Median	Cell 1	Cell 2	Cell 3	Cell 4	Cell 5	Cell 6
RSP	vs. Cell 1	102	—					
	vs. Cell 2	70	**	—				
	vs. Cell 3	114	NS	***	—			
	vs. Cell 4	93	NS	*	NS	—		
	vs. Cell 5	100	NS	*	NS	NS	—	
	vs. Cell 6	95	NS	NS	NS	NS	NS	—
	Median	8.3	0.55	12	3.3	4.9	0.80	
SolPM		Median	1.3	0.15	1.8	0.91	0.77	0.25
Nicotine	vs. Cell 1	1.3	—					
	vs. Cell 2	0.15	***	—				
	vs. Cell 3	1.8	**	***	—			
	vs. Cell 4	0.91	NS	***	**	—		
	vs. Cell 5	0.77	NS	***	***	NS	—	
	vs. Cell 6	0.25	***	NS	***	***	***	—
	Median	1.0	0.50	1.9	0.93	0.81	0.50	
Cotinine		Median	1.0	—				
Cotinine	vs. Cell 1	0.50	***	—				
	vs. Cell 2	1.9	**	***	—			
	vs. Cell 3	0.93	NS	***	**	—		
	vs. Cell 4	0.81	NS	**	***	NS	—	
	vs. Cell 5	0.50	*	NS	***	NS	NS	—
	vs. Cell 6	—						

Cell 1 = Smoking household; Cell 2 = non-smoking household; Cell 3 = smoking household/smoking workplace; Cell 4 = smoking household/non-smoking workplace; Cell 5 = non-smoking household/smoking workplace; Cell 6 = non-smoking household/non-smoking workplace; NS = not significant ($p > 0.05$).

* $p \leq 0.05$; ** $p \leq 0.01$; *** $p \leq 0.001$.

pervasion of outdoor air into the indoor locations studied in Beijing. For all the other analytes investigated, the Kruskal-Wallis ANOVA provided evidence of a significant overall difference between Cells, and subsequent pairwise comparisons of Cells were performed using the Wilcoxon rank sum test (table 8). Since Cell comparisons using UVPM measurements were virtually identical to those for RSP, highlighting the non-tobacco-specific nature of this marker in Beijing, Wilcoxon rank sum test

findings were not reported for UVPM. Similarly, comparisons using 3-EP were not reported, the behaviour of this analyte closely mimicking that reported for nicotine.

Median 24-hour TWA RSP concentrations found in this study varied between 70 and $114 \mu\text{g} \cdot \text{m}^{-3}$, with Cell 2 (housewives from non-smoking homes) being the only Cell with concentrations significantly lower than any others. These concentrations were the highest we have found to date and were up to 5.3 times higher than median levels

in any of the European or other Asian cities studied. They were also up to 6.4 times higher than those found in the recent 16-city US study [13]. Particles collected for RSP determination in this study had a median cut-off point of approximately 3.5 μm ($\text{PM}_{3.5}$). It was noted that over 90% of subjects from smoking workplaces (Cells 3 and 5) in Beijing were exposed to 24-hour TWA RSP levels above $50 \mu\text{g}\cdot\text{m}^{-3}$. The proposed European threshold limit for particulates (PM_{10}) is $50 \mu\text{g}\cdot\text{m}^{-3}$, which level should not be exceeded more than 7 times in a year.

The highest median level of ETS particles (SolPM) was determined for subjects living in smoking households and working in smoking workplaces (Cell 3, $12 \mu\text{g}\cdot\text{m}^{-3}$). The concentrations found for Cell 3 were not significantly different ($p > 0.05$) from those found for Cell 1 (housewives from smoking households), but were significantly higher ($p \leq 0.05$) than all other Cells. In all other cities previously studied by the authors, subjects in Cell 3 have been exposed to the highest levels of ETS particles, with median levels in Europe varying from $3.0 \mu\text{g}\cdot\text{m}^{-3}$ in Stockholm to $35 \mu\text{g}\cdot\text{m}^{-3}$ in Barcelona. The concentrations found for Cell 3 in the other Asian cities studied were considerably lower than those found in Beijing, with median levels of $2.6 \mu\text{g}\cdot\text{m}^{-3}$ and $1.5 \mu\text{g}\cdot\text{m}^{-3}$ found in Hong Kong and Kuala Lumpur, respectively. Housewives from non-smoking homes (Cell 2), and workers living and working in non-smoking environments (Cell 6) were exposed to the lowest levels of ETS particles in this study, with median values below $1 \mu\text{g}\cdot\text{m}^{-3}$. Overall, the median levels of ETS particles found for the various Cells in Beijing appeared to more closely resemble those found in Europe, in particular in Turin, Paris and Prague, and were considerably higher than those found in other Asian cities or in the recent 16-city US study [13]. Median ETS particle levels for the highest exposed group (Cell 3) in Beijing represented less than 11% of total RSP. Previously, we had found a 34% contribution of ETS particles to RSP in Barcelona [5], the European city with the highest measured ETS and RSP levels. This indicates that RSP from sources other than ETS should be reduced in order to effect the greatest benefit in Beijing's air quality.

The highest median nicotine concentration ($1.8 \mu\text{g}\cdot\text{m}^{-3}$) was again found for Cell 3, with measured levels being significantly higher ($p \leq 0.01$) than for all other Cells. The lowest levels were measured for Cell 2, housewives living with non-smokers (median $0.15 \mu\text{g}\cdot\text{m}^{-3}$), although these were not significantly different ($p > 0.05$) from Cell 6 (median $0.25 \mu\text{g}\cdot\text{m}^{-3}$).

Saliva Cotinine

Saliva cotinine concentrations, expressed as an average of pre- and post-monitoring levels, are reported by Cell in table 7. The measured concentrations mirrored those for SolPM and nicotine, with office workers living and working with smokers (Cell 3, median $1.9 \text{ ng}\cdot\text{ml}^{-1}$) having significantly higher ($p \leq 0.01$) levels than all other Cells.

It was not intended that cotinine should be used as either a qualitative or quantitative marker for an individual's ETS exposure in this study, and over half of the samples analysed had cotinine concentrations below the LOQ ($1.0 \text{ ng}\cdot\text{ml}^{-1}$). However, the median levels reported were consistent with the measured levels of ETS particles and nicotine, suggesting the applicability of saliva cotinine measurements as a marker for ETS exposure in a study population. The use of a method with an improved LOQ may provide, for example, statistical significance between groups of subjects with low levels of exposure (e.g. Cells 5 and 6). Cotinine measurements used for ETS exposure estimates inherit the inadequacies of nicotine behaviour [23] and a number of other uncertainties including dietary influences [24] and metabolic differences [25, 26]. In addition, there is no validated analytical method in the public domain suitable for the quantification of cotinine in saliva, or other body fluids, at concentrations below $0.1 \text{ ng}\cdot\text{ml}^{-1}$. Bernert et al. [27] have recently reported a method for the determination of cotinine in human serum with a claimed limit of detection of $0.05 \text{ ng}\cdot\text{ml}^{-1}$. Based upon their reported data, this method would appear to have an LOQ of approximately $0.2 \text{ ng}\cdot\text{ml}^{-1}$, which represents a significant improvement on published methods to date.

Exposures to RSP, ETS Particles and Nicotine

The term 'exposure' is frequently used in the scientific literature, often in a way that is confusing and subject to numerous definitions. When used in studies relating to airborne pollutant concentrations, exposure is normally determined by fixed-site monitoring over standard time periods. In the context of this series of personal monitoring studies, where concentrations cannot be directly related to a specific environment, we have used the term 'potential inhaled quantity' (PIQ), a measure of 'total exposure'. PIQs were calculated as the product of the analyte concentration, the length of time the individual was subjected to such concentration and the breathing rate maintained throughout the period. Zartarian et al. [28] have recently reviewed the literature relating to exposure definitions and have proposed a glossary of terms to establish a common language. According to their proposals, the

term 'intake dose' is equivalent to PIQ as used in this study. Where PIQs have been quoted in terms of CEs, these have been calculated in relation to the mainstream particle (tar) and nicotine yields of typical cigarettes; it is recognised, however, that the particle phases of ETS and mainstream smoke differ considerably in composition and particle size. The nicotine and particulate yields of local Chinese cigarettes were not available, and the values of 12 mg ETS particles and 1 mg nicotine were used. These substituted values were calculated from the mean yields of the top six selling cigarette brand types in each of the eight European countries we have studied. In this paper, calculated CE values are used solely for conceptual comparison of PIQs between groups of non-smokers. In this context, the factor used to relate exposures of non-smokers to smokers [29] was not required.

The PIQs during the monitoring period were calculated using the same procedures as previously [1, 2, 9-11]. The concentrations and sampling times for each subject were determined from their individual monitors and an 'awake' breathing rate of $0.65 \text{ m}^3 \cdot \text{h}^{-1}$ for females and $1.05 \text{ m}^3 \cdot \text{h}^{-1}$ for males [30] was assumed at all times. These 'awake' breathing rates were calculated as the average of typical 'light-work' and 'rest' breathing rates. It is recognised that breathing rates will be lower when subjects are asleep; however, at these times, the ETS concentrations may be lower than the TWA concentrations, as determined by their personal monitor, due to the absence of active smoking. Conversely, breathing rates will be higher during any period of activity, and these periods may correspond to higher ETS concentrations. Median and 90th percentile PIQs were subsequently calculated for each Cell from these individually calculated values in order to represent 'typical' and 'highly exposed' subjects, respectively. Daily PIQs of RSP, ETS particles and nicotine, calculated for each Cell as detailed above, are summarised in table 9. A comparison of PIQs for Cells 4 and 5 would suggest that, on a daily basis, the ETS exposure contribution from a smoking workplace is greater than that of a smoking home in Beijing.

In order to estimate annual exposure, separate procedures were adopted for housewives and for workers. The annual PIQ for each housewife (Cells 1 and 2) was calculated by assuming they were exposed to their measured concentrations for an entire year, and that a breathing rate of $0.65 \text{ m}^3 \cdot \text{h}^{-1}$ was maintained at all times. For workers (Cells 3-6), the annual PIQ for each subject was calculated from the data provided by the separate monitors worn in the workplace and away from the workplace. Male and female working subjects were assumed to have

Table 9. Estimated PIQs for all subjects during the 24-hour monitoring period

Cell	RSP μg	ETS particles μg	Nicotine μg
<i>Median PIQs</i>			
1 (SH)	1.607	131	21
2 (NSH)	1.089	8.6	2.4
3 (SH, SW)	2.172	192	32
4 (SH, NSW)	1.908	60	14
5 (NSH, SW)	2.183	105	15
6 (NSH, NSW)	1.445	12	5.0
<i>90th percentile PIQs</i>			
1 (SH)	3.516	1,051	56
2 (NSH)	2,416	45	11
3 (SH, SW)	4,148	1,354	87
4 (SH, NSW)	3,404	493	58
5 (NSH, SW)	4,729	917	63
6 (NSH, NSW)	4,582	110	15

PIQs were calculated for each individual using the sampling times and air concentrations determined from their individual monitors. A breathing rate of $0.65 \text{ m}^3 \cdot \text{h}^{-1}$ was assumed for females and $1.05 \text{ m}^3 \cdot \text{h}^{-1}$ for males at all times.

SH = Smoking household; NSH = non-smoking household; SW = smoking workplace; NSW = non-smoking workplace.

breathing rates of $1.05 \text{ m}^3 \cdot \text{h}^{-1}$ and $0.65 \text{ m}^3 \cdot \text{h}^{-1}$, respectively, at all times and to spend 35 h per week and 48 weeks per year in the workplace. Calculation of annual PIQs for all subjects assumed no variation in ETS marker concentrations throughout the year, including weekends, from those measured during the monitoring period. Median and 90th percentile PIQs by Cell, calculated from the estimated annual PIQs, using the above assumptions, are reported in table 10 together with estimates of ETS particle and nicotine PIQs in terms of CEs.

Ranking Cells by median for annualised ETS particle and nicotine PIQ shows Cell 3 > Cell 1 > Cell 5 > Cell 4 > Cell 6 > Cell 2. With the exception of Cell 1, this ranking was very similar to that found by us in most of the other cities studied. Housewives from smoking homes (Cell 1) had previously been found to be ranked 3rd or 4th in the other cities we studied. Cell 1 subjects in Beijing would therefore appear to have higher exposures to ETS relative to similar subjects in other cities. Based upon median PIQs of ETS particles and nicotine (table 10), the most exposed subjects would potentially inhale between 5 and 11 CEs per year (CEs/y), and the least exposed, housewives living with non-smokers, would receive consider-

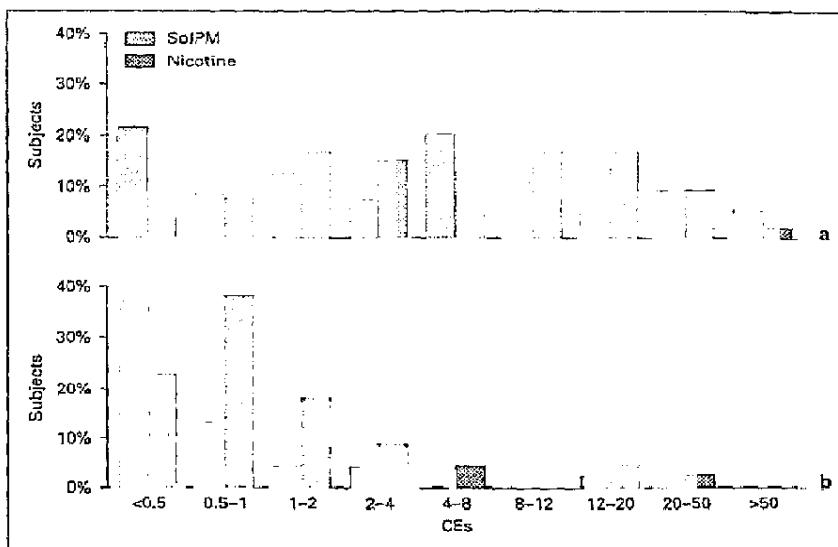


Fig. 5. Estimated annual CE distributions for housewives. **a** Cell 1 (smoking home). **b** Cell 2 (non-smoking home).

Table 10. Estimated annual PIQs for all subjects

	Annual PIQ, mg			CEs	
	RSP	ETS particles	nicotine	ETS particles	nicotine
<i>Median PIQs</i>					
1 (SH)	584	48	7.7	4.0	7.7
2 (NSH)	396	3.2	0.85	0.26	0.85
3 (SH, SW)	776	60	11	5.0	11
4 (SH, NSW)	710	27	5.5	2.3	5.5
5 (NSH, SW)	812	30	4.6	2.5	4.6
6 (NSH, NSW)	576	4.9	1.4	0.41	1.4
<i>90th percentile PIQs</i>					
1 (SH)	1,259	381	20	32	20
2 (NSH)	917	16	4.1	1.4	4.1
3 (SH, SW)	1,720	549	32	46	32
4 (SH, NSW)	1,278	204	20	17	20
5 (NSH, SW)	1,739	235	14	20	14
6 (NSH, NSW)	1,730	32	4.1	2.6	4.1

Breathing rates of $0.65 \text{ m}^3 \cdot \text{h}^{-1}$ for females and $1.05 \text{ m}^3 \cdot \text{h}^{-1}$ for males were assumed at all times. Annual PIQs for subjects in Cells 1-2 were calculated from their measured air concentrations as follows: Individual annual PIQ = air concentration $\times (0.65) \times 24 \times 365$.

ETS marker concentrations for workers at work and outside the workplace were calculated from the data provided by the 'work' and 'home' monitors. Annual PIQs for individuals in Cells 3-6 were calculated as follows, assuming a 35-hour working week and 48-week working year with the remainder of the time spent outside the workplace: Individual annual PIQ = 'work' concentration $\times (0.65 \text{ or } 1.05) \times 35 \times 48 + \text{'home' concentration} \times (0.65 \text{ or } 1.05) \times [(24 \times 365) - (35 \times 48)]$.

Median and 90th percentile data were determined for each cell from the individual PIQs as determined above.

SH = Smoking household; NSH = non-smoking household; SW = smoking workplace; NSW = non-smoking workplace.

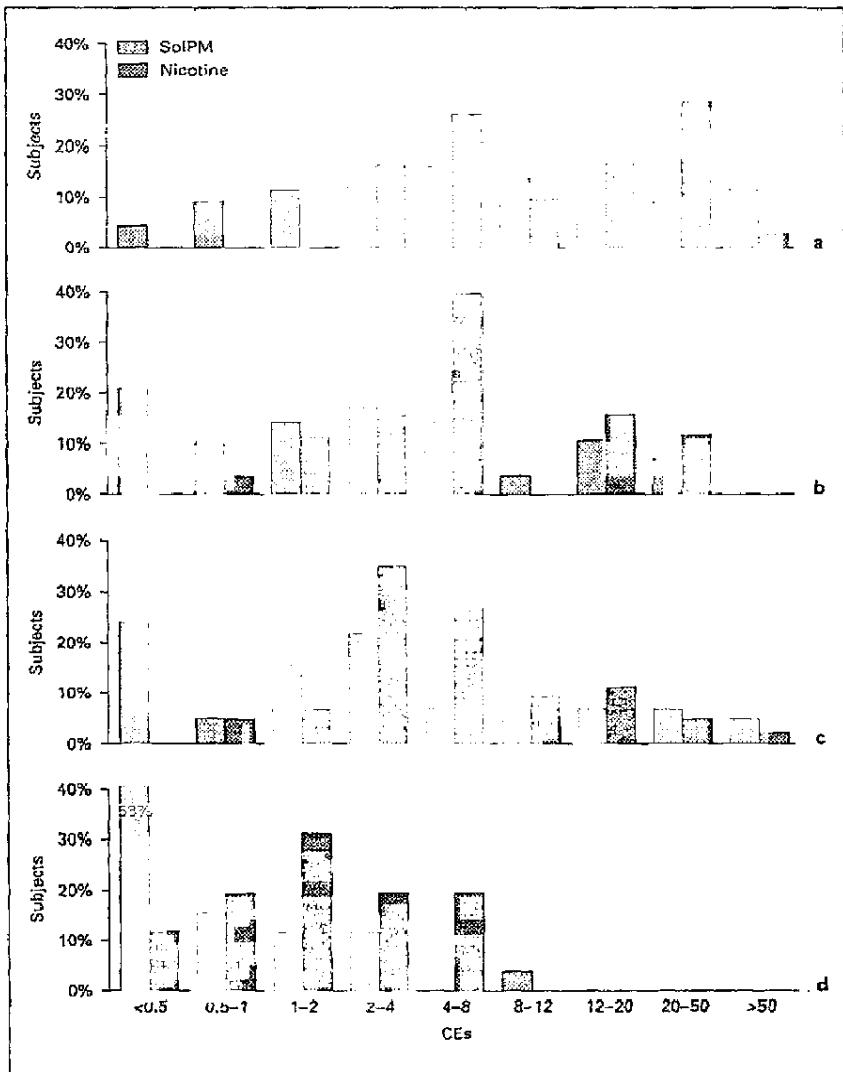


Fig. 6. Estimated annual CE distributions for office workers. **a** Cell 3 (smoking home/smoking workplace). **b** Cell 4 (smoking home/non-smoking workplace). **c** Cell 5 (non-smoking home/smoking workplace). **d** Cell 6 (non-smoking home/non-smoking workplace).

ably less than 1 CE/y. The most highly exposed (90th percentile levels) non-smokers in this study, workers who lived and worked with smokers, would potentially inhale to between 32 (nicotine) and 46 (SolPM) CEs/y. Conversely, if they came from non-smoking households and workplaces, they would receive less than 4.1 CEs/y.

The distributions of estimated annual PIQs of ETS particles and nicotine for housewives and office workers, by Cell, are depicted in figures 5 and 6. The data for SolPM and nicotine have been normalised to depict PIQs in terms of CEs/y, and both show a very wide range of

estimated exposures. The two estimates show different distribution patterns, with SolPM estimates being considerably 'flatter' and covering a somewhat wider range than those for nicotine. These observations indicate the need to obtain ETS exposure data using several different measures wherever possible. Currently, the available markers provide estimates, and further research may provide the 'ideal' marker. These figures also highlight the potential error in using any point estimate (e.g. median) for reporting exposure data, and may indicate that simple exposure calculations, as performed in this and other similar stud-

Table 11. Estimated contribution of the workplace to annual RSP, ETS particle and nicotine exposures for all working subjects

Cell	RSP %	ETS particles %	Nicotine %
3 (SH, SW)	28 (18)	38 (32)	42 (26)
4 (SH, NSW)	19 (12)	29 (33)	15 (21)
5 (NSH, SW)	30 (19)	56 (34)	59 (24)
6 (NSH, NSW)	23 (19)	32 (26)	38 (22)

Contributions are reported as the mean (SD in parentheses) of percent annual PIQs at work for all subjects. PIQs were calculated assuming measured concentrations from each individual subject's monitors were maintained throughout the year, and the subjects spent 35 h per week and 48 weeks per year at work.

SH = Smoking household; NSH = non-smoking household; SW = smoking workplace; NSW = non-smoking workplace.

It was also possible, by applying the same criteria used for the calculations in table 10, to estimate the contribution of the workplace to overall annual exposure for each subject. A summary of these estimates, expressed as the mean percent contribution (standard deviation in parentheses) by Cell, is presented in table 11. For subjects exposed at home and at work, these estimates show that the workplace would contribute an average of approximately 40% of annual exposure to nicotine and ETS particles. Offices in Beijing where smoking was allowed were estimated to be a major contributor to annual ETS exposure. For the largest group of workers in this study, those from non-smoking homes, mean annual ETS contribution from those workplaces was between 56 and 59%.

Acknowledgments

The funding for this study was made available to Covance Laboratories Ltd. by the Center for Indoor Air Research (CIAR), Linthicum, Md., USA. Thanks go to research nurse Eva Götharsson at the Karolinska Institute, Göran Tamm and Christer Hermansson at MarknadsAnalys and to the Department of Biopharmaceutical Analysis at Covance Laboratories Ltd. where all the samples were analysed.

References

- Phillips K, Howard DA, Bentley MC, Alván G: Assessment of environmental tobacco smoke and respirable suspended particle exposures of non-smokers in Hong Kong using personal monitoring. *Environ Int* 1998;24:851-870.
- Phillips K, Bentley MC, Howard DA, Alván G: Assessment of environmental tobacco smoke and respirable suspended particle exposures for non-smokers in Kuala Lumpur using personal monitoring. *J Exp Anal Environ Epidemiol*, in press.
- Phillips K, Howard DA, Bentley MC, Alván G: Assessment by personal monitoring of respirable suspended particles and environmental tobacco smoke exposure for non-smokers in Sydney, Australia. *Indoor Built Environ* 1998;7:188-203.
- Phillips K, Bentley MC, Howard DA, Alván G: Assessment of air quality in Stockholm by personal monitoring of non-smokers for respirable suspended particles and environmental tobacco smoke. *Scand J Work Environ Health* 1996;22(suppl 1):1-24.
- Phillips K, Bentley MC, Howard DA, Alván G, Huici A: Assessment of air quality in Barcelona by personal monitoring of non-smokers for respirable suspended particles and environmental tobacco smoke. *Environ Int* 1997;23:173-196.
- Phillips K, Howard DA, Bentley MC, Alván G: Assessment of air quality in Turin by personal monitoring of non-smokers for respirable suspended particles and environmental tobacco smoke. *Environ Int* 1997;23:851-871.
- Phillips K, Bentley MC, Howard DA, Alván G: Assessment of air quality in Paris by personal monitoring of non-smokers for respirable suspended particles and environmental tobacco smoke. *Environ Int* 1998;24:405-423.
- Phillips K, Howard DA, Bentley MC, Alván G: Measured exposures by personal monitoring for respirable suspended particles and environmental tobacco smoke of housewives and office workers resident in Bremen, Germany. *Int Arch Occup Environ Health* 1998;71:201-212.
- Phillips K, Howard DA, Bentley MC, Alván G: Assessment of environmental tobacco smoke and respirable suspended particle exposures for non-smokers in Lisbon by personal monitoring. *Environ Int* 1998;24:301-324.
- Phillips K, Howard DA, Bentley MC, Alván G: Assessment of environmental tobacco smoke and respirable suspended particle exposures for non-smokers in Basel by personal monitoring. *Atmos Environ*, in press.
- Phillips K, Bentley MC, Howard DA, Alván G: Assessment of environmental tobacco smoke and respirable suspended particle exposures for non-smokers in Prague by personal monitoring. *Int Arch Occup Environ Health* 1998;24:379-390.
- Heavner DL, Morgan WT, Ogden MW: Determination of volatile organic compounds and respirable particulate matter in New Jersey and Pennsylvania homes and workplaces. *Environ Int* 1996;22:159-183.
- Jenkins RA, Palausky A, Counts RA, Bayne CK, Dindal AB, Guerin MW: Exposure to environmental tobacco smoke in sixteen cities in the United States as determined by personal breathing zone air sampling. *J Exp Anal Environ Epidemiol* 1996;6:473-502.

14 Sterling EM, Collett CW, Ross JA: Assessment of non-smokers' exposure to environmental tobacco smoke using personal-exposure and fixed-location monitoring. *Indoor Built Environ* 1996;5:112-125.

15 Baek SO, Kim YS, Perry R: Indoor air quality in homes, offices and restaurants in Korean urban areas - Indoor/outdoor relationships. *Atmos Environ* 1997;31:529-544.

16 Ogden MW, Heavner DL, Foster TL, Maiolo KC, Cash SL, Richardson JL, Martin P, Simmons PS, Conrad FW, Nelson PR: Personal monitoring system for measuring environmental tobacco smoke exposure. *Environ Technol* 1996;17:239-250.

17 Ogden MW, Maiolo KC, Oldaker GB, Conrad FW: Evaluation of methods for estimating the contribution of ETS to respirable suspended particles. International Conference on Indoor Air Quality and Climate, Ottawa 1990. *Indoor Air '90* 1990;2:415-420.

18 Van Yunakis H, Cijka HB, Lagone JJ: Method 16 - Radioimmunoassay for nicotine and cotinine; in O'Neill IK, Brunnemann KD, Dodet B, Hoffman D (eds): *Environmental Carcinogens: Methods of Analysis and Exposure Measurement*. Lyon, International Agency for Research on Cancer, World Health Organisation, 1987, pp 317-330.

19 Ogden MW, Eudy JW, Heavner DL, Conrad FW, Green CR: Improved gas chromatographic determination of nicotine in environmental tobacco smoke. *Analyst* 1989;114:1005-1008.

20 Nelson PR, Conrad FW, Kelly SP, Maiolo KC, Richardson JD, Ogden MW: Composition of environmental tobacco smoke (ETS) from international cigarettes and determination of ETS-RSP: Particulate marker ratios. *Environ Int* 1997;23:47-52.

21 Phillips K, Howard DA, Browne D, Lewisley JM: Assessment of personal exposures to environmental tobacco smoke in British non-smokers. *Environ Int* 1994;20:693-712.

22 Nelson PR, Heavner DL, Collie BB, Maiolo KC, Ogden MW: Effects of ventilation and sampling time on environmental tobacco smoke component ratios. *Environ Sci Technol* 1992;26:1909-1915.

23 Nelson PR, Heavner DL, Oldaker GB III: Problems with the use of nicotine as a predictive environmental tobacco smoke marker. *Measurement of Toxic and Related Air Pollutants*, Environmental Protection Agency/Air and Waste Management Association International Symposium. Pittsburgh, Air and Waste Management Association, 1990, pp 530-555.

24 Davies RF, Stiles MF, DeBethizy JD, Reynolds JH: Dietary nicotine: A source of urinary cotinine. *Food Chem Toxicol* 1991;29:821-827.

25 Cholerton S, Arpanahi A, McCracken N, Bousfield C, Taber H, Johnstone E, Leathart J, Daly AK, Idle JR: Poor metabolisers of nicotine and CYP2D6 polymorphism. *Lancet* 1994;343:62-63.

26 Benowitz NL, Jacob P, Sachs DPL: Deficient C-oxidation of nicotine. *Clin Pharmacol Ther* 1995;57:590-594.

27 Bernert JT, Turner WE, Pirkle JL, Sosnoff CS, Atkins JR, Waldrep MK, Ann Q, Covey TR, Whitfield WE, Gunter EW, Miller BB, Patterson DG, Needham LL, Hannon WH, Sampson EJ: Development and validation of sensitive method for determination of serum cotinine in smokers and nonsmokers by liquid chromatography/atmospheric pressure ionization tandem mass spectrometry. *Clin Chem* 1997;43:2281-2291.

28 Zartarian VG, Ott WR, Duan N: A quantitative definition of exposure and related concepts. *J Exp Anal Environ Epidemiol* 1997;7: 411-437.

29 Ogden MW: Environmental tobacco smoke exposure of smokers relative to non-smokers. *Anal Commun* 1996;33:197-198.

30 Holcomb LC: Indoor air quality and environmental tobacco smoke: Concentration and exposure. *Environ Int* 1993;19:9-40.